HDAC inhibitors - pushing HIV out of hiding

In people who have been taking ART for several years and who have no other co-infections, HIV-infected cells produce very few copies of HIV and appear to infect other cells at a relatively low rate. In many of these cases, HIV can lie dormant (latent) in cells that are resting, until stimulated from time to time. As part of an attempt at curing HIV, it would be important to rid the body of these infected cells. Driving HIV out of hiding in these cells is sometimes called “purging latently infected cells” by researchers.

Several years ago Canadian researchers attempted to cure HIV by giving ART users the anti-seizure drug valproic acid in addition to ART. However, this did not work.

Introducing...

Valproic acid belongs to a class of drugs called HDAC (histone deacetylase) inhibitors. Since that Canadian trial, researchers have pondered using more potent HDAC inhibitors, such as the following:

- panobinostat
- romidepsin
- vorinostat

Clinical trials with these drugs are underway in Australia, Western Europe and the U.S. in HIV-positive people to assess their impact.

The return of Antabuse

The drug Antabuse (disulfiram) is used to treat some people with alcohol addiction, as it causes highly unpleasant reactions when they drink alcohol. In the body, disulfiram is converted into another compound called ditiocarb (Imuthiol, diethyldithiocarbamate). Results of laboratory experiments with cells suggest that this compound has antifungal and anti-parasite and possibly anti-HIV activity. Clinical trials in the late 1980s and early ’90s led to mixed results, and the drug was never approved by regulatory authorities for use as an HIV treatment.

At present, researchers are having another look at disulfiram because in laboratory experiments with cells it appears to activate latent HIV.

Bryostatin

An even older drug, bryostatin, was also studied in the 1980s for its impact on HIV-infected cells. In recent years, researchers have found that bryostatin and closely related compounds can have beneficial effects that may make them useful for cure research. In particular, bryostatin appears to be able to coax HIV from latency in different types of cells of the immune system.

For the future

It is likely that future attempts at curing HIV will require multiple and perhaps novel therapies. Just what those therapies ought to be is still being debated by scientists. In this issue of TreatmentUpdate, we explore several attempts at bringing HIV out of latency in ART users with HDAC inhibitors.

—Sean R. Hosein

REFERENCES:


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